Title

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CLINICAL VIGNETTE

Nephrogenic Diabetes Insipidus due to Incomplete Urinary Tract Obstruction

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Introduction

A 73-year-old female was admitted for nausea, vomiting, and abdominal pain. She developed hypernatremia and polyuria in the hospital with increasing serum sodium despite supplemental D5W prompting nephrology consultation. She reported poor oral intake with frequent vomiting over the past week, and no passage of stool for a month. She had a history of rectosigmoid adenocarcinoma 2 years prior to the current admission, which initially presented with bowel obstruction. Initial treatment consisted of neoadjuvent chemo, surgical excision, and then adjuvant chemo and radiation for the next 9 months. She was then lost to follow up but re-presented about 1 month prior to admission with vaginal discharge with CT scan showing a 7.5 x 6.6 cm necrotic mass arising from the sigmoid colon suture line associated with a probable rectovaginal fistula. There was no history of prior kidney disease, and she had normal kidney function on admission.

She was diagnosed with obstruction of the small and large intestines and underwent open laparotomy on hospital day 4. Extensive local tumor recurrence and left hydroureter were noted, and a colostomy was created and drains were placed.

Blood pressures were stable throughout the hospitalization. Medications given during the hospitalization included amlodipine, docusate, gastrografin, enoxaparin, iodinated IV contrast for CT scans (hospital days 1, 9, and 12), lorazepam, magnesium sulfate, metoclopramide, labetalol, ondansetron, pantoprazole, piperacillin/tazobactam (days 10-21), potassium chloride, and vancomycin (days 9-11); vancomycin trough on day 11 was 9.5. TPN was given on days 15-21.

Her serum creatinine started to increase on hospital day 10 and peaked at 1.6 mg/dL on hospital day 16. The sodium parameters changed over a similar time course. Urine specific gravity 3 weeks prior to admission was 1.024, but when the patient developed hypernatremia, the urine concentration was inappropriately low. On hospital day 10, the serum sodium as well as the urine output started increasing. On day 14, the urinalysis had 52 RBC, sodium concentration of 63 mmol/L, and a fractional excretion of sodium of 1.8%. D5W was started on the evening of day 14. On day 16, the urine osmolality increased from 170 to 216 after 1mcg of DDAVP.

Repeat urinalysis was otherwise unremarkable, and urine sodium was 56 mmol/L. The serum sodium on hospital day 16 was 158 mmol/L. Table 1 summaries and trends the laboratory parameters.

Table 1. Laboratory testing during the development of acute kidney injury and hypernatremia.

Parameter	D9	D10	D11
Urine output per 24h (mL)	1400	2900	2700
Sodium (mmol/L)	136	137	143
Creatinine (mg/dL)	0.5	0.6	0.7
Urine SG		1.007	
Urine Osm			
Ddavp (mcg)			
Hctz (mg)			

Parameter	D12	D13	D14	D15
Urine output per 24h (mL)	3100	5800	2800	4275
Sodium (mmol/L)	141	145	158	156
Creatinine (mg/dL)	0.8	1.4	1.6	1.5
Urine SG			1.007	
Urine Osm				
Ddavp (mcg)				
Hctz (mg)				

Parameter	D16	D17	D18	D22
Urine output per 24h (mL)	6900	3625	4300	2025
Sodium (mmol/L)	149	151	145	138
Creatinine (mg/dL)	1.4	1.4	1.3	1.3
Urine SG	1.005			
Urine Osm	170	332	337	
Ddavp (mcg)	1	2		
Hctz (mg)		12.5	12.5	12.5

On admission, contrast CT showed only simple kidney cysts. On hospital day 9, repeat contrast CT showed interval development of bilateral hydronephrosis and hydroureter extending down to the pelvis but then obscured. HCTZ 12.5 mg and DDAVP 2 mcg were given on day 17; urine osmolality two hours post-dose was 332. HCTZ 12.5 mg daily was continued without additional DDAVP dosing, and on day 18, the urine osmolality was 327; on day 18 D5W urine replacement was discontinued. Ureteral stenting was attempted on day 23, but the bladder was found to have diffuse infiltration most likely due to malignancy. Neither ureteral orifice was successfully localized. On day 24, the creatinine was 1.2, and sodium was 138. The patient was tolerating an oral diet and off IV fluids and foley.

Discussion

As is often seen in cases of acute kidney injury, more than one insult occurred in this patient, leading to acute kidney injury from contrast and from urinary obstruction. She also received medications known to cause acute interstitial nephritis (pantoprazole and piperacillin), but the time course and lack of pyuria along with lack of other allergic symptoms made this unlikely. The fractional excretion of sodium was equivocal (greater than 1%), but fractional excretions of sodium of less than 1% are more typically seen in pure contrast-induced nephropathy. The preserved urine output indicated that the obstruction was not complete, but the hypernatremia, dilute urine, and minimal response to exogenous DDAVP are consistent with nephrogenic diabetes insipidus.[1] After starting HCTZ, the urine became more concentrated, the D5W was weaned off, and the hypernatremia resolved. The creatinine recovered incompletely, indicative of recovery from CIN but ongoing incomplete obstruction.

Obstruction of urine outflow leads to multiple types of tubular dysfunction.[2] Diabetes insipidus (DI) is an important manifestation of tubular dysfunction seen in urinary obstruction as it can lead to rapid rises in serum sodium if a complete urine obstruction is suddenly relieved. However, DI can also occur during an incomplete obstruction when urine output is maintained,[3-4] which is consistent with this patient's clinical course. Animal models have shown that aquaporins are down regulated in kidneys with obstructed urine outflow[2,3] and that there are other ways in which the distal tubular response to salt delivery and to ADH is altered.[5] Thiazide diuretics are useful in treating nephrogenic diabetes insipidus because they lead to decreased urine free water excretion due to ADH independent mechanisms.[6] Thiazides will lead to an increase in urinary osmolality by impairing urinary dilution in the distal tubule and by stimulating hypovolemia-induced increase in proximal sodium and water reabsorption, thereby diminishing water delivery to the ADH-sensitive sites in the collecting tubules and reducing the urine output. Non-steroidal anti-inflammatory (NSAID) drugs and amiloride can also be used, the latter being most useful in cases of lithium toxicity as it inhibits lithium uptake into the cells of the distal tubule.[5,6] The efficacy of NSAIDs is due to inhibition of renal prostaglandin synthesis as prostaglandins antagonize the action of ADH.[7]

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